amended. The amendments to claim 53 are supported in the application, e.g., on page 50, lines 9-13.

Claim 53 is rejected under 35 U.S.C. § 101 as allegedly being directed to nonstatutory subject matter. (Office Action mailed June 3, 2002, page 3). According to the Office, the claim 53 encompasses all naturally occurring antibodies to metalloproteinase inhibitors and does not involve the "hands of man." (*Id.*)

Without acquiescing in the rejection, Applicants have amended claim 53 to indicate that the antibody is "isolated and purified," as suggested by the Examiner. Applicants respectfully request reconsideration and withdrawal of the rejection of claim 53 under 35 U.S.C. § 101.

Claims 53-56 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. (Office Action, page 4). According to the Office, the specification provides "[n]o written description of what structurally constitutes any specific epitope required to make a functional monoclonal antibody and their corresponding hybridoma cell line. . .." (*Id.*) The Office appears to interpret a statement on page 19 of the specification ("each monoclonal antibody is directed against a single determinant on the antigen") as requiring knowledge of what those determinants are in order to describe the claimed monoclonal antibodies. (*Id.*)

Applicants respectfully traverse this rejection. Because of the amendment to claim 53, claim 53 and dependent claims 54-56 encompass antibodies and hybridoma

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

cell lines secreting antibodies that bind specifically to the polypeptides depicted in Figures 1 and 2. The specification states that both polyclonal and monoclonal antibodies that bind to those sequences are part of the invention. *See, e.g.,* Specification, page 18, line 31, to page 19, line 17. Applicants respectfully suggest that the Office is mistakenly reading a phrase in the specification, which describes a difference between monoclonal and polyclonal antibodies, into a requirement that the monoclonal antibodies of the invention are made to a single specific epitope.

The complete sentence that the Office partially quotes reads:

> In contrast to conventional antibody (polyclonal) preparations which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody is directed against a single determinant on the antigen.

Specification, page 18, line 36, to page 19, line 4. This is undoubtedly a property of monoclonal antibodies, but in no way requires that one know the amino acid sequence of the epitope in order to describe the antibody. Applicants are unaware of any controlling legal authority for the proposition that an adequate written description of a monoclonal antibody requires a description of the amino acid sequence to which that antibody binds.

All that *is* necessary to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, is that the specification convey to one skilled in the art that the applicants were in possession of the claimed invention at the time of filing. *See Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). Example 16 of the Synopsis of Application of Written Description Guidelines (available on the Office's web site) is instructive. That Example considers whether a specification that

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

teaches the isolation, purification, and characterization of Antigen X satisfies the written description requirements for claims drawn to antibodies that specifically bind to Antigen X. According to Example 16, "[t]he specification contemplates but does not teach in an example antibodies which specifically bind to Antigen X." Thus the specification in Example 16 provides less description of antibodies than Applicants' specification, which describes the generation of polyclonal antibodies to human TIMP-2. *See* Example 6 of the Specification, pages 48-50.

Example 16 of the Synopsis of Application of Written Description Guidelines concludes:

> Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.
>
> **Conclusion**: The disclosure meets the requirement under 35 USC 112 first paragraph as providing an adequate written description of the claimed invention.

Here, Applicants' specification teaches the isolation, purification, and characterization of the proteins depicted in Figures 1 and 2. The specification clearly contemplates that polyclonal and monoclonal antibodies to these proteins are part of the invention and provides a working example teaching how to make polyclonal antibodies. The Office provides no evidence that one skilled in the art would doubt that Applicants were in possession of the antibodies and hybridomas encompassed by claims 53-56, which contain no limitation reciting specific epitopes. Thus, Applicants respectfully

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

request reconsideration and withdrawal of the rejection of claims 53-56 for lack of written description.

Claims 53-56 are also rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. (Office Action, page 5). The Office acknowledges that the specification enables the preparation of polyclonal antibodies directed to the proteins depicted in Figures 1 and 2. (*Id.*) According to the Office, however, the specification "does not reasonably provide enablement for making monoclonal antibodies with unknown epitopes or hybridoma cell lines putatively 'secreting' such." (*Id.*) The Office also asserts that because the term "metalloproteinase inhibitor alone sets forth no structural characterization and little functional characteristics for one of ordinary skill in the art on how to make and use such a protein", it would require undue experimentation to make specific antibodies. (*Id.*)

Applicants respectfully traverse. One skilled in the art would recognize that the term "metalloproteinase inhibitor" in claim 53 means a protein with the structural and functional characteristics of the human and bovine TIMP-2 proteins described in the specification. However, solely to advance prosecution, Applicants have amended claim 53 to recite "a polypeptide selected from the amino acid sequence set out in FIG. 1 or in FIG. 2" rather than "metalloproteinase inhibitor."

The Office has acknowledged that the specification enables one skilled in the art to make polyclonal antibodies to these proteins. (Office Action, page 5.) However, the Office again appears to assert that in order to enable one skilled in the art to make

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

monoclonal antibodies and hybridomas, the disclosure must teach particular desirable antigen-specific epitopes. (Office Action, page 6: "the specification does not teach which particular amino acids are critical for detecting any metalloproteinase inhibitor protein's function, or what amino acid residues constitute a 'metalloproteinase inhibitor'-specific epitope.")

Applicants' claims are drawn to antibodies and hybridomas secreting antibodies that bind specifically to the polypeptides depicted in Figures 1 and 2. The claims contain no limitation that requires the antibodies to bind to particular epitopes, and the Office provides no evidence that one skilled in the art would require information concerning particular epitopes in order to make the claimed antibodies without undue experimentation.

As the Federal Circuit made clear in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), making monoclonal antibodies to a known and well-characterized antigen does not involve undue experimentation. Here, the Office provides no evidence to support the conclusion that one skilled in the art would be forced to engage in undue experimentation in order to make the monoclonal antibodies encompassed by the rejected claims. For these reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 53-56 under 35 U.S.C. § 112, first paragraph.

Finally, claims 53, 54, and 56 are rejected under 35 U.S.C. § 102(e) as allegedly being unpatentable over U.S. Patent No. 5,595,885 to Stetler-Stevenson et al. ("Stetler-Stevenson") (Office Action, page 7). According to the Office, Stetler-Stevenson teach antibodies made to TIMP-2 "in which specific peptide sequences/epitopes are described

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

to make monoclonal antibodies . . .." (*Id.*) The Office further contends that, since hybridoma cells are required to make monoclonal antibodies, Stetler-Stevenson also teaches the limitations of claim 56. (*Id.*)

Applicants respectfully traverse. Anticipation under 35 U.S.C. § 102 requires that "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros., Inc. v. Union Oil Co.*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). If the reference does not expressly set forth a particular element of the claim, that reference still may anticipate if that element is "inherent" in its disclosure. To establish inherency, the Office must show "that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. v. Monsanto Co.*, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991).

In fact, Stetler-Stevenson never mentions monoclonal antibodies and, therefore, cannot expressly anticipate claims 54 and 56. The Office simply asserts that, because Stetler-Stevenson indicate that peptide fragments of their human protein can be used as immunogens, this references teaches monoclonal antibodies. As the Office must certainly be aware, peptide fragments can be used as immunogens for the preparation of polyclonal antibodies. The Office has failed to provide any evidence that "persons of ordinary skill" would recognize that "the missing descriptive matter is necessarily present in" Stetler-Stevenson's reference to peptides as immunogens.

Moreover, Applicants have attached their Declaration Under 37 C.F.R. § 1.131 showing that their invention of the claimed subject matter recited by claim 53 predates

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Stetler-Stevenson's earliest possible priority date, March 21, 1988. For this reason, Stetler-Stevenson's disclosure is not prior art to claim 53. Applicants respectfully request reconsideration and withdrawal of the rejection of those claims under 35 U.S.C. § 102(e).

Applicants respectfully requests the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: October 16, 2002

By: _____
William L. Strauss
Reg. No. 47,114

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

APPENDIX TO AMENDMENT OF OCTOBER 16, 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Amendments to the Claims

53. (ONCE AMENDED) An isolated and purified antibody, wherein said antibody binds specifically to [metalloproteinase inhibitor] a polypeptide comprising an amino acid sequence of FIG. 1 or in FIG. 2.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com